

AMENDMENTS TO THE SPECIFICATION:

Please delete the paragraph on page 6, line 5 and replace it with the following paragraph:

The human peptide sequence of HARP₁₃₆ is also presented in sequence SEQ ID N^o NO: 1.

Please delete the paragraph on page 6, lines 20-25 and replace it with the following paragraph:

In a preferred manner, the fragments 13-39, 65-97 or 111-136 are the fragments as enumerated in the sequence SEQ ID N^o NO: 1, namely the sequences :

13-39 : SDCGEWQWSVCVPTSGDCGLGTREGTRT (SEQ ID N^o NO: 2)

65-97 : AECKYQFQAWGECDLNTALKTRTGSLKRALHNA (SEQ ID N^o NO: 3)

111-136 : KLTKPKPQAESKKKKKEGKKQEKMLD (SEQ ID N^o NO: 4).

Please delete the paragraph on page 8, lines 30-31 and replace it with the following paragraph:

The fragments of SEQ ID N^o NO: 2 and SEQ ID N^o NO: 3 containing respectively the unit 18-23 WQWSVC (Residues 6-11 of SEQ ID NO: 2) or the unit 71-77 FQAWGEC (Residues 7-13 of SEQ ID NO: 3) are of particular interest.

Please delete the paragraph on page 11, lines 1-5 and replace it with the following paragraph:

The nucleic acid which is useful for the production of recombinant peptide can in particular have the following sequences:

- sequence coding for the peptide 13-39 (SEQ ID N° NO: 5)
- sequence coding for the peptide 65-97 (SEQ ID N° NO: 6)
- sequence coding for the peptide 111-136 (SEQ ID N° NO: 7).

Please delete the paragraphs on page 11, lines 10-20 and replace them with the following paragraphs:

These nucleic acids can be defined as comprising :

- i) sequences similar to at least 70 %, preferably at least 80 %, preferably at least 90 %, even at least 95 % of the sequence SEQ ID N° NO: 5, N° SEQ ID NO: 6 or N° SEQ ID NO: 7 ; or
- ii) sequences which hybridise with the sequence SEQ ID N° NO: 5, N° SEQ ID NO: 6 or N° SEQ ID NO: 7 or its complementary sequence under strict hybridisation conditions, or
- iii) sequences which code for the reference peptide as defined above.

In a preferred manner, such a homologous nucleotide sequence hybridises specifically with the complementary sequences of the sequence SEQ ID N° NO: 5, N° SEQ ID NO: 6 or N° SEQ ID NO: 7 under strict conditions. The parameters defining the conditions of strictness depend upon the temperature at which 50% of the paired

strands separate (Tm).

Please delete the paragraph on page 12, lines 6-10 and replace it with the following paragraph:

Therefore a homologous nucleotide sequence includes any nucleotide sequence which differs from the sequence SEQ ID N° NO: 5, N° SEQ ID NO: 6 or N° SEQ ID NO: 7 by mutation, insertion, deletion or substitution of one or more bases, or by the degeneracy of the genetic code, in so far as it codes for a peptide having the biological activity of the fragments of HARP to which they refer.

Please delete the paragraph on page 17, lines 21-24 and replace it with the following paragraph:

A preferred pharmaceutical composition comprises :

- the peptide 13-39 of sequence SEQ ID N° NO: 2 ;
- the peptide 65-97 of sequence SEQ ID N° NO: 3 ; and
- the peptide 111-136 of sequence SEQ ID N° NO: 4.

Please delete the paragraph on page 18, lines 5-9 and replace it with the following paragraph:

A preferred composition comprises:

- a nucleic acid coding for the peptide 13-39 of sequence SEQ ID N° NO: 2 ;

- a nucleic acid coding for the peptide 65-97 of sequence
SEQ ID N^o NO: 3 ;

- a nucleic acid coding for the peptide 111-136 of sequence
SEQ ID N^o NO: 4.

Please delete the paragraph on page 25, lines 19-29 and replace it with the following paragraph:

Fibroblast cells of type NIH 3T3 are cultured at a density of 3×10^4 cells per cm^2 in DMEM culture medium supplemented with 10% of foetal calf serum. After 24 hours of incubation at 37°C in an atmosphere containing 7 % of CO_2 , the culture medium is replaced by DMEM which does not contain foetal calf serum. Twenty-four hours afterwards, the HARP molecule (4 nM) in the presence or absence of the HARP peptides 16-48 or 65-97 of respective sequences SEQ ID N^o NO: 2 and ~~N^o~~ SEQ ID NO: 3 at a concentration ranging from 0.1 to 10 μM is added over 18 hours. After this period of incubation, 0.5 μCi of [methyl- ^3H]thymidine is added and 6 hours afterwards the cells are fixed by a 10% solution of trichloroacetic acid. The radioactivity incorporated by the cells is then counted by liquid scintillation after having effected a cell lysis with a solution of sodium hydroxide at a concentration of 0.1 N.

Please delete the paragraph on page 26, lines 11-20 and replace it with the following paragraph:

The capacity of the peptide P111-136 (SEQ ID ~~N°~~ NO: 4) to inhibit tumour angiogenesis has been tested by inducing tumour growth by injection of PC3 cells into nude mice in the presence or absence of peptide P111-136. 2×10^6 PC3 cells are injected into groups of 5 nude mice (nude/nude, Laboratoire IFFA CREDO) treated or not by injection in the region of the tumour of 100 μ l per day of a solution of PBS (control group) or by a solution of peptide P111-136 diluted in PBS at a concentration of 5 mg/kg. On day 9, 13, 16, 20, 23 and 27 the size of the tumour is measured with the aid of a calliper gauge. The results are presented in Figure 3 and indicate that the HARP peptide 111-136 used at a dose of 5 mg per kg induces an inhibition of the growth of the tumours.

Please delete the paragraph on page 27, lines 14-22 and replace it with the following paragraph:

MDA-MB-231 cells from human mammary carcinoma are cultured at a density of 3×10^3 cells per cm^2 in a DMEM culture medium containing 10% of foetal calf serum, 0.35% of agar and containing or not containing concentrations of HARP peptides 13-39 and 65-97 (SEQ ID ~~N°~~ NO: 2 and ~~N°~~ SEQ ID NO:3). The cells are cultured in a culture box with 12 wells (35 mm in diameter/well) previously covered with 1 ml of 0.6% agar. The peptides are added into the culture medium every 2 days. After 13 days of incubation in a humid atmosphere at 37°C and 7% CO_2 , the colonies having a

diameter equal to or greater than 50 μ m are counted. Each point in the experiment is carried out in triplicate and each experiment is repeated three times.

Please delete the paragraph on page 28, lines 1-4 and replace it with the following paragraph:

As HARP is a growth factor implicated in the proliferation and the differentiation of endothelial cells, the inventors have, in the experiment set out below, studied the effect of the HARP peptides 13-39 and 65-97 (SEQ ID N^o NO: 2 and ~~N^o~~ SEQ ID NO: 3) on the angiogenic activity induced by HARP.